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Traditionally, a microbial population has been considered homogeneous in optimization studies of fermentation processes. However, research has shown that a typical microbial population in a fermenter is heterogeneous. There are indications that such heterogeneity may be both beneficial (facilitates quick adaptation to new conditions) and harmful (reduces yields and productivities) (Bylund *et al.* (1998); Enfors *et al.* (2001)). Significant gradients of e.g. dissolved oxygen, substrates, and pH are typically observed in many industrial scale fermentation processes. Consequently, the microbial cells experience rapid changes in environmental conditions as they circulate throughout the reactor, which might pose stress on the cells, affect their metabolism and consequently affect the level of heterogeneity of the population.

To further investigate these phenomena and gain a deeper understanding of population heterogeneity, a *Saccharomyces cerevisiae* growth reporter strain based on the expression of green fluorescent protein (GFP) was constructed which allows to perform single cell analysis, and thereby created the possibility to map population heterogeneity.

A factorial design experiment of the growth reporter strain demonstrated a highly dynamic behaviour with regards to subpopulation distribution during the different growth stages. To simulate which effect glucose gradients, often seen in large scale cultivations, have on population heterogeneity, glucose perturbations during continuous cultivation of the growth rate reporter strain was performed and the physiological changes were analysed on a single cell level. From the simulation experiment it could be demonstrated that glucose had a clear influence on subpopulation distribution.

References

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